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Implications of prioritizing HIV cure: new momentum to overcome old challenges in HIV

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Abstract

Background: Curing HIV is a new strategic priority for several major AIDS organizations. In step with this new priority, HIV cure research and related programs are advancing in low, middle, and high-income country settings. This HIV cure momentum may influence existing HIV programs and research priorities.

Discussion: Despite the early stage of ongoing HIV cure efforts, these changes have directly influenced HIV research funding priorities, pilot programs, and HIV messaging. The building momentum to cure HIV infection may synergize with strategic priorities to better identify adults and infants with very early HIV infection. Although HIV cure represents a new goal, many existing programs and research techniques can be repurposed towards an HIV cure. HIV messages focused on engaging communities towards an HIV cure need to be careful to promote ARV adherence and retention within the HIV continuum of care.

Summary: An increased emphasis within the AIDS field on finding an HIV cure has several important implications. Strengthening connections between HIV cure research and other areas of HIV research may help to catalyze research and facilitate implementation in the future.

Keywords: HIV, Cure, Policy, Social science

Background

HIV cure research and related programs are accelerating around the world. This new priority developed over the last five years because of an increased understanding of the long-term side effects of lifelong antiretroviral therapy (ART), the public health challenges of current strategies, and basic science advances regarding HIV latency [1]. The goal of curing HIV infection is a strategic priority for the National Institutes of Health National Institute for Allergy and Infectious Diseases [2], the International AIDS Society [1], and other organizations. There are over 100 ongoing HIV cure research studies underway around the world [3].

Although the field of HIV cure is still in its infancy and many decisions about cure efforts or pilot programs have not been centrally organized, there are already important

implications of expanding HIV cure momentum [4]. The purpose of this article is to describe these implications and to suggest ways that pilot programs could maximally synergize with existing research and programs. We examine how HIV cure programs, especially research, have started to gradually influence funding priorities, pilot programs for very early HIV detection, and HIV messaging.

Discussion

The most substantial implication of the increased emphasis of the AIDS field on finding a cure for HIV is changing HIV research priorities. The International AIDS Society HIV cure resources tracking group estimated that 157.9 million USD was invested in HIV cure research in 2014 [5]. These investments from the public sector (139.9 USD) and philanthropies (17.0 million USD) are likely an underestimate because they did not capture growing private sector contributions. A range of public sector funding agencies in high-income countries have prioritized HIV cure research, including the United States National Institutes of Health [2, 6], the Medical Research Council, the

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French National Agency for AIDS Research, and the Canadian Institutes of Health Research [7]. In addition to high-income country support, there have been special programs to support HIV cure research in China [8], Thailand [9], and Cuba [10]. The National Institutes of Health in the United States has been the single largest funder of HIV cure research to date, accounting for 72 % of the 2014 research funds [5]. The American Foundation for AIDS Research announced a total of 100 million USD in grants to support HIV cure research [11]. The University of North Carolina at Chapel Hill and GlaxoSmithKline recently formed a new public-private partnership to cure HIV, supported by 20 million dollars from GlaxoSmithKline over the course of 4 years [12].

The new emphasis on HIV cure within broader HIV funding priorities raises an important question about the relationship between HIV cure and other HIV research priorities. The International AIDS Society “Towards a Cure” initiative has explicitly stated that the global HIV response should not divert research funding from other areas of HIV research towards cure, instead arguing for greater HIV cure resources [5]. In addition to greater resources for HIV cure research, there is a need for integrative research that crosses disciplinary boundaries [4] and brings together HIV cure and other existing HIV priorities.

Another important policy implication of the HIV cure momentum is enhanced detection of adults and adolescents with acute or very early HIV infection. The first few weeks or months after infection, but prior to seroconversion, constitute the period of acute HIV infection [13]. We define very early HIV infection to include the 6 months following viral acquisition. Adults and adolescents diagnosed and treated during very early HIV infection are critical for HIV cure research [14]. Such individuals are important because they likely have smaller reservoirs [14], decreased viral replication [15] and genetic diversity [16] sustained T-cell and B-cell function [17, 18], better immune restoration potential, lack of extended inflammatory responses and comorbidities associated with chronic HIV infection [19], and no or limited previous exposure to antiretrovirals (ARVs). As a result, individuals with very early HIV infection would likely be easier to cure and recruited for enrollment in HIV cure research studies. Yet the implementation of testing programs to identify very early HIV infections has been challenging [20]. High cost (especially for small laboratories), logistical problems, and the brevity of very early HIV infection further complicate the detection of this phase of HIV infection in many settings. HIV cure strategies for those with very early HIV infection and those with chronic HIV infection will both be important.

New HIV cure momentum also provides an opportunity to synergize and extend existing programs focused on identifying very early HIV infected individuals. Programs seeking to increase or improve diagnosis and treatment during very early infection are driven by both public health imperatives and concerns for long-term patient well-being. Public health programs focused on identifying very early HIV infection have been established because of the increased risk of onward transmission during very early infection [21]. Additionally, the advantages of early diagnosis and suppression of viremia [15, 17–19, 22–24] add impetus to efforts to introduce and retain these patients in care. HIV cure-based scientific interest in early immune response, HIV disease progression, and the establishment and perpetuation of latent HIV reservoirs may add further momentum to these efforts if increased numbers of very early infected and/or ARV suppressed participants are required for research participation. Recently, the Treatment Action Group identified twelve HIV cure research studies around the world already enrolling HIV infected individuals during acute or very early infection [3].

Although the additional momentum created by HIV cure research is unlikely to overcome logistical problems, HIV cure may provide another strong reason to enhance detection of very early HIV infected adults within clinical trial sites. HIV cure related interest in very early infection may help to raise awareness about acute HIV infection, its symptoms, and why early detection and suppression are important. This would be useful given that many patients [25] and primary care providers [26] still lack of knowledge and awareness about very early infection.

In addition to enhanced detection of very early infected adults and adolescents, HIV cure momentum may increase the number of neonates discovered with very early HIV infections. Neonates who acquire HIV infection from their mothers are another key group for HIV cure research efforts as demonstrated by the extended remission of the Mississippi child case [27]. Analogous to adults and adolescents with early infection, this context provides an opportunity in which there is likely a smaller reservoir [28] and may be more amenable to clinical cure research [29]. At the same time, early detection of neonates with newly acquired HIV infection is similarly hampered by a range of problems that include lack of reliable reservoir biomarkers, delays in diagnosis, and insufficient mechanisms to effectively recruit newly infected neonates.

Finally, HIV cure has progressively changed how we talk about HIV in public health messages. Although the resources necessary for implementing HIV control strategies are substantial, available HIV resources have been stable or decreasing in many regions [30, 31]. The field of HIV cure has brought new energy to the HIV field, including scholars, policymakers, and advocates. Qualitative research

among HIV-infected individuals has shown that HIV cure research could spark new hope for healing, decreasing barriers to HIV testing and improving retention through the care continuum [32]. One HIV cure community engagement project at the University of North Carolina integrated HIV cure alongside testing, prevention, and other related community HIV campaigns [33]. At the same time, these messages should be cautious and create realistic expectations about the timeframe for development of an HIV cure [34, 35].

Summary

Given the opportunity presented by a growing HIV cure momentum around the world, we have several recommendations for enabling these policy-program synergies. First, engaging a wide range of global HIV stakeholders, especially in low and middle income settings, will be important for realizing the programmatic synergies articulated above, just as it was in the development of previous interventions [36]. Policymakers make critical decisions about implementation and linkages between research and programs. Second, integrating HIV cure within existing test and treat priorities will help strengthen existing linkages and prevent the development of false dichotomies, such as that which occurred between HIV prevention and treatment in the 1990s [37]. Third, optimizing health systems for very early detection of HIV-infected adults, adolescents, and neonates would be beneficial for both individual clinical and public health outcomes. Finally, the HIV cure global framework requires strengthening multisectoral linkages between clinicians, policymakers, advocates, and other stakeholders in order to develop a comprehensive plan for curing HIV in the future [4].

Conclusion

HIV cure momentum is building in a range of global settings. While this is a new priority, there are several ways that research towards an HIV cure can strengthen existing HIV policies and practices.

Competing interests

The authors declare no competing interests.

Authors' contributions

JDT and MV conceived the original idea for this article. JDT led the writing with substantial help from AG and YL. All authors made substantial contributions to the writing of this manuscript and approved the final manuscript.

Authors' information

The co-authors are part of a working group examining the social science and ethics of HIV cure research. More information about our working group is available here: <http://searchiv.web.unc.edu/>.

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